

## **REMARKS/ARGUMENTS**

### **The Status of the Claims.**

Claims 1, 3-7, 12-15, 34-44 and 53-54 are pending with entry of this amendment. Claims 8-11 have been cancelled. Cancellation of these claims is without prejudice, without intent to abandon any originally-claimed subject matter, and without intent to acquiesce in any rejection of record. Applicants expressly reserve the right to file one or more continuing applications containing these cancelled claims.

Claims 1, 3-7, 12-13, 39-42, and 53 are amended herein. These amendments are made without prejudice and are not to be construed as abandonment of the previously claimed subject matter or agreement with any objection or rejection of record. These amendments introduce no new matter and support is replete throughout the specification. With respect to claims 3, 5, and 40, support for conservative substitutions can be found throughout the specification at, for example, page 2, line 24 through page 3, line 7; page 8, line 26 through page 9, line 5; page 13, lines 14-23, and in the claims as originally filed. With respect to claims 4 and 39, support for the sequence identity determination can be found throughout the specification at, for example, page 11, lines 8-26. Claims 34 and 53 are amended to remove the reference to cancelled claim 16. Claims 1, 6, 7, 12, 13, 41 and 42 are amended to further clarify the claimed invention.

Applicants submit that no new matter has been added to the application by way of the above Amendment. Because the amendments place the claims in condition for allowance, or simplify issues for appeal, entry of the amendment, pursuant to 37 C.F.R. § 1.116 is respectfully requested.

### **Interview Summary**

Applicants respectfully thank the Examiner for the helpful telephonic interview held March 18, 2004. An Interview Summary is submitted herewith in accordance with 37 CFR § 1.133(b) and MPEP 713.04.

### **Oath/Declaration**

The Examiner has alleged that the Oath/Declaration is defective because the phrase "as amended by any amendment specifically referred to above" is missing from the text. As discussed in the telephonic Interview held March 18, 2004, no amendments were made to the claims prior to review and signature of the application paperwork by the inventors. Applicants note that the

declaration was signed by the inventors on May 20 and May 31, 1999; the first amendment to the claims (addressing sequence listing requirements) was filed June 7, 1999. Since no amendments were made to the specification or claims prior to signature by the inventors, Applicants submit that the Oath/Declaration is not defective, and respectfully request that the Examiner accept the signed document filed June 7, 1999.

**35 U.S.C. §112, First Paragraph.**

Claims 3-13 and 39-42 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed. Applicants respectfully traverse to the extent that the rejections apply to the claims as amended.

Claims 3-7, 12-13, and 39-42 have been amended to further clarify the claimed invention, as helpfully suggested by the Examiner in the telephonic interview held March 18, 2004. Applicants respectfully request that the rejection be withdrawn.

**35 U.S.C. §103(a).**

**THE CLAIMS ARE PATENTABLE OVER XU, BIRD AND CHAUDHARY**

Claims 1, 34-38 and 53-54 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Xu et al. (Int. J. Cancer 53:401-408, 1993) and further in view of Bird et al. (Science 242:423-426, 1998) and Chaudhary et al. (PNAS 87:1066-1070, 1990). The rejection was originally made in the Office Action mailed 3/17/03 (paper 27) and was maintained by the Examiner in the Action mailed 12/31/03. Applicants traverse.

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. In re Royka, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). The cited art (alone or in combination) does not teach every element of the claimed invention. Claim 1 is drawn to antibodies that a) are single chain, b) are internalizing and c) specifically bind to a specified epitope on the c-erbB2 receptor that is recognized by F5 (SEQ ID NO:1) or C1 (SEQ ID NO:2). Claim 34 is drawn to chimeric molecules that specifically binds a cell bearing a c-erbB-2 antigen, said chimeric molecule comprising an effector molecule attached to an antibody of claim 1. Claim 54 is drawn to compositions comprising a pharmacological excipient and the antibody of claim 1 or the chimeric molecule of claim 34.

Xu is alleged to teach or describe hybridomas and antibodies produced from the hybridomas; the antibodies are alleged to be internalizing and capable of binding to c-erbB2, but are not single chain antibodies. Bird and Chaudhary are alleged to teach methods for preparation of single chain antibodies. However, the cited publications (alone or in combination) do not teach or disclose antibodies that bind to the epitope recognized by F5 and C1. This conclusion is supported by the accompanying expert Declaration. In brief, since the Xu antibodies elicit a different cellular response (e.g., a considerably lower rate of internalization), one of skill in the art would surmise that the Xu antibodies bind to a different epitope than the epitope bound by F5 and C1. Thus, Xu et al. does not teach or disclose antibodies that bind to the epitope recognized by F5 and C1. Neither Bird nor Chaudry remedy this deficit.

Applicants maintain that the claimed invention is not rendered unpatentable over Xu et al. further in view of Bird et al. and Chaudhary et al. because the cited references in combination do not teach the limitations of the claims. Applicants respectfully request that this rejection be withdrawn.

#### THE CLAIMS ARE PATENTABLE OVER MAIER, BIRD AND CHAUDHARY

Claims 1, 34-38 and 53-54 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Maier et al. (Cancer Res. 51:5361-5369, 1991) and further in view of Bird et al. (Science 242:423-426, 1998) and Chaudhary et al. (PNAS 87:1066-1070, 1990). Applicants traverse to the extent that the rejection applies to the claims as amended.

As noted above, to establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. The cited art (alone or in combination) does not teach every element of the claimed invention. Maier is alleged to teach internalizing antibodies that bind to c-erbB2. Bird and Chaudhary are alleged to teach methods for preparation of single chain antibodies. However, the cited publications (alone or in combination) do not teach or disclose antibodies that bind to the epitope recognized by F5 and C1, as provided by the accompanying expert Declaration. Since the Maier antibodies elicit a different cellular response (e.g., a considerably lower rate of internalization), one of skill in the art would surmise that the Maier antibodies bind to a different epitope than the epitope bound by F5 and C1. Thus, Maier et al. does not teach or disclose antibodies that bind to the epitope recognized by F5 and C1. Neither Bird nor Chaudry remedy this deficit.

Applicants maintain that the claimed invention is not rendered unpatentable over Maier et al. further in view of Bird et al. and Chaudhary et al. because the cited references in

combination do not teach the limitations of the claims. Applicants respectfully request that this rejection be withdrawn.

THE CLAIMS ARE PATENTABLE OVER SHAWVER, BIRD AND CHAUDHARY

Claims 1, 34-38 and 53-54 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Shawver et al. (Cancer Res. 54:1367-1373, 1994) and further in view of Bird et al. (Science 242:423-426, 1988) and Chaudhary et al. (PNAS 87:1066-1070, 1990). Applicants traverse to the extent that the rejection applies to the claims as amended.

As noted above, to establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. The cited art (alone or in combination) does not teach every element of the claimed invention. Shawver is alleged to teach internalizing antibodies that bind to c-erbB2. Bird and Chaudhary are alleged to teach methods for preparation of single chain antibodies. However, the cited publications (alone or in combination) do not teach or disclose antibodies that bind to the epitope recognized by F5 and C1, as provided by the accompanying expert Declaration. Since the Shawver antibodies elicit a different cellular response (e.g., a considerably lower rate of internalization), one of skill in the art would surmise that the Shawver antibodies bind to a different epitope than the epitope bound by F5 and C1. Thus, Shawver et al. does not teach or disclose antibodies that bind to the epitope recognized by F5 and C1. Neither Bird nor Chaudry remedy this deficit.

Applicants maintain that the claimed invention is not rendered unpatentable over Shawver et al. further in view of Bird et al. and Chaudhary et al. because the cited references in combination do not teach the limitations of the claims. Applicants respectfully request that this rejection be withdrawn.

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### CONCLUSION

In view of the foregoing, Applicants believes all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

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Respectfully submitted,



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#### Attachments:

- 1) A petition to extend the period of response for **2** months;
- 2) A transmittal sheet;
- 3) A fee transmittal sheet;
- 4) Interview Summary
- 5) Expert Declaration and accompanying expert Biographical Sketch;
- 6) Notice of Appeal; and
- 7) A receipt indication postcard.